

K
Hap
September 27, 1958

Dear Hilary:

I hope you had a most pleasant trip in Europe. I sent you the pen you admired a little while ago, and hope you have excellent use of it, and write as well as ever.

I should have written you sooner, but this has been my first moment of composure. Everything is going very well here and at Stanford, but there have been a number of time-consuming distractions.

First: In re the antibody program. I had promised to send you the antigen and protocols for the Salmonella experiment. However, I think it would be better judgment to wait for the ~~present~~ perfection of another system. Becca Patras is a postdoctoral fellow from Haurowitz' lab, spending the year here with Bill Stone and myself. She is working on a system of immune hemolysis of cattle red cells (sensitized with complement) that this promises to be considerably more satisfactory than immobilization in a number of respects. The sensitivity is quite promising; the reaction is readily scored in microdroplets, and there is the possibility of quantitating the response in terms of the percentage of cells lysed at dilutions near titre. Equally important, the antigen is mosaic and there is the possibility of using test antigens of related serotypes to determine fairly rapidly what range of antibodies are being formed by single cells. Rabbits have given quite satisfactory specific sera, but we still have to investigate mice and rats; we should use isogenic strains as far as possible. We may possibly try to induce tolerance to the 'species antigens' as a means of sharpening the specificity of the responses, and this already suggests a number of approaches to test the 'hypermutable' hypothesis. (Should that be called 'hypermutable with retrospective election' to completely conceal what I mean.)

As you can see from the mimeographed postscript I sent you recently, the form of the proposal has been modified slightly. After considerable thought I realized how little the revision really deviated from Burnet's idea and felt this should be stressed, rather than obscuring the relationship with the more generalized terminology of 'transition'. (I have also seen some of Talmage's writing along the same lines. But Talmage does not have an explicitly drawn model, especially for tolerance.)

Item 2: From all you and several other informants have told me, I conclude that it would not be possible for us to choose better than Silvers among the younger men in this country. It might be wiser to wait; however, a number of other aspects of planning (e.g. to get a firm lien on space and funds) will be

easier if we have a more tangible plan for staff, even if this is ~~my~~ quite tentative and subject to mutual agreement. So I am thinking of approaching him (on such a basis) quite soon. I imagine you will be of two minds about this, not to want to lose a good man, but I know you well enough to be certain that you would be more concerned for his own interests, as he sees them for himself. Anything you can tell me now that would make our negotiations as straightforward as possible, so as to cause him minimum distraction from his work, would be to maximum advantage all the way around. I had in mind to offer him an Assistant Professorship in Genetics at a salary of about \$9,000 ± which could take effect within any reasonable time after next July. It might be possible to squeeze something more for him, but on the whole I do not believe it would be best either for the department or himself for the sake of what would certainly be only a temporary advantage. If you think this is an unrealistic scale we may have to review the whole question again.

I had had a rather vain hope of interesting Av' Mitchison in a comparable arrangement but it seems quite definite that he and Lorna have no interest in leaving Britain. But I am hotter than ever on the idea of developing 'histogenetics' and I think now we might be able to develop it more broadly with two more junior appointments instead, say Silvers plus a fresh postdoctoral associate whose interests were in tissue culture. (Harry Eagle has mentioned one or two possibilities). With Henry Kaplan and Cliff Grobstein on both sides, histogenetics should have a promising future at Stanford, but I am still waiting for the preliminary plans for 'Wistar-West': just say the word if there is ever anything I can do to help.

Anyhow, I will wait to hear from you before proceeding any further. Your position in this is so ambiguous as perhaps to be no longer amusing, but I think we might be able to save Silvers a good deal of confusion, and after my own experience last year I would not wish it on anyone!

Yours, as ever,

Joshua Lederberg

P.S. Once we have a lab set up and running, I think histogenetics might be fostered even if we don't get what we want by permanent staff, and there might be some reciprocal advantage in having visiting professorships to interact with us in genetics. But to forestall the question why I don't plunge into this myself, I have neither the energy nor experience to do the setting up of the lab. routine, training assistants and so forth. If we get a regular appointee, I certainly wouldn't want to meddle in his program but his establishment would make it much more feasible to expand with joint projects in areas outside his own immediate interests.

P.P.S. I hope histogenetics is an acceptable term for 'genetic analysis of somatic tissue cells' more broadly than histocompatibility genetics.